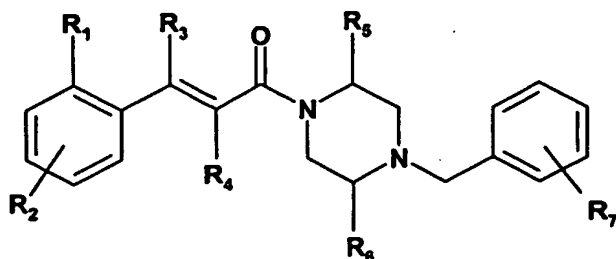


CLAIMS

1. A compound of formula i, or a pharmaceutically acceptable salt or ester thereof,



wherein

R_1 is $-X-R_{10}$, $-X-(R_{10})_2$ or $-NR_{11}R_{12}$

Wherein X is a linker comprising 1 atom or a chain comprising 2, 3 or 4 atoms selected from N, C, O or S, and wherein when said linker comprises 2 or more C atoms the linker may comprise 1 or more C=C or C≡C bonds;

wherein any of said atoms has up to 2 optional substituents selected from hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, sulfur amino;

R_{10} is a substituent independently selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, cycloalkyl, heterocycloalkyl, aryl, heteroaryl;

R_{11} and R_{12} each represent a lower alkyl group connected together such that R_1 is an optionally substituted heterocycloalkyl or heteroaryl group;

R_2 and R_7 represent one or more substituents attached to the phenyl ring selected from the group consisting of hydrogen, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl, heteroaryl or a substituent forming a bicyclic ring system of which the phenyl ring to which it is attached forms part of the bicycle for example butadiene forming naphthyl, or heterobutadiene forming quinolinyl, quinoxalinyl or isoquinolinyl;

R_3 and R_4 are independently selected from the group consisting of hydrogen, cyano, halo, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl;

R_5 and R_6 are independently selected from the group consisting of hydrogen, cyano, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on X are one or more independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, amino, sulfur, sulfinyl, sulfonyl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro, oxy, lower alkyl, lower alkyenyl, lower alkynyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R_{10} are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, Sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R_{11} and R_{12} are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R_2 and R_1 are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R_3 and R_4 are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo,

nitro, oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

The optional substituents on R_5 and R_6 are one or more substituents independently selected from the group consisting of hydrogen, oxo, cyano, hydroxyl, optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, cycloalkyl, heterocycloalkyl, aryl, imino, oxime;

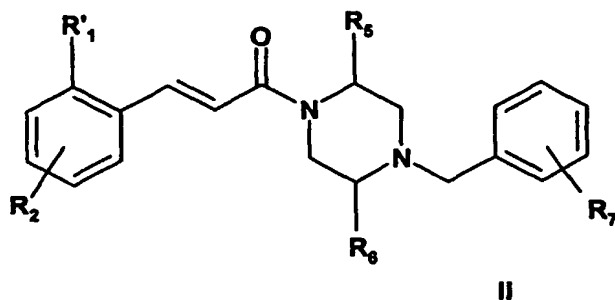
Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, hydroxyl, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or optionally substituted oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, oxo, cyano, halo, nitro or oxy, lower alkyl, lower alkyenyl, lower alkynyl, carbonyl, amino, sulfur, cycloalkyl, heterocycloalkyl, aryl;

2. a compound of formula II, or a pharmaceutically acceptable salt or ester thereof,



Wherein

R'_1 is $-X'-R'_{10}$

Wherein X' is a linker independently selected from optionally substituted $-N-C-N-$, $-N-C-$, $-N-S-$, $-N-S-N-$, $-C-N-$, $-S-N-$, $-C\equiv C-$, $-C=C-$, $-N-C-S-$, $-C-$, $-S-\underset{|}{N}-S-R'_{10}$.

Wherein $R_2 - R_{10}$ are as herein before defined.

R'_{10} is one or more substituents independently selected from the group consisting of hydrogen, halo, or optionally substituted carbonyl, amino, heterocycloalkyl and aryl.

when R'_1 is $-N-C-N-R'_{10}$ the C atom is substituted by oxo, $=N-C\equiv N$ or $=C-NO_2$.

when R'_1 is $-N-C-N-R'_{10}$, R'_{10} is Hydrogen.

when R'_1 is $-N-C-N-R'_{10}$, R'_{10} is optionally substituted by hydrogen.

when R'_1 is $-N-C-R'_{10}$ or $-C-N-R'_{10}$ the C atom is substituted by oxo.

when R'_1 is $-N-C-R'_{10}$ or $-C-N-R'_{10}$, R'_{10} is optionally substituted methyl, piperidinyl, imidazolidinyl, pyrrolidinyl, morpholino.

when R'_1 is $-N-C-R'_{10}$ or $-C-N-R'_{10}$, R'_{10} is substituted by hydrogen, methyl, benzyl, acetyl, oxo, dimethylamino, isopropyl, hydroxy, formic acid ethyl ester.

when R'_1 is $-N-S-R'_{10}$ or $R'_{10}-S-\underset{|}{N}-S-R'_{10}$ the S atom or atoms are substituted twice by oxo.

when R'_1 is $-N-S-R'_{10}$ or $R'_{10}-S-\underset{|}{N}-S-R'_{10}$, R'_{10} is optionally substituted methyl.

when R'_1 is $-N-S-R'_{10}$ or $R'_{10}-S-\underset{|}{N}-S-R'_{10}$, R'_{10} is optionally substituted by hydrogen.

when R'_1 is $-N-S-N-R'_{10}$ the S atom is substituted twice by oxo and the N atom is independently optionally substituted by methyl.

when R'_1 is $-N-S-N-R'_{10}$, R'_{10} is hydrogen or optionally substituted methyl, imidazolyl, thiazolyl.

when R'_1 is $-N-S-N-R'_{10}$, R'_{10} is optionally substituted by hydrogen, methyl, acetamidyl.

when R'_1 is $-C\equiv C-R'_{10}$, R'_{10} is optionally substituted methyl, isopropyl or piperidinyl

when R'_1 is $-C\equiv C-R'_{10}$, R'_{10} is optionally substituted by hydrogen or amine

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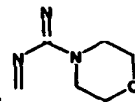
when R₁ is -C=C-R₁₀, R₁₀ is optionally substituted piperidinyl

when R₁ is -C=C-R₁₀, R₁₀ is optionally substituted by hydroxy, methyl.

when R₁ is -N-C-S-R₁₀ the C atom is substituted by =N-C≡N or

when R₁ is -N-C-S-R₁₀, R₁₀ is optionally substituted methyl

when R₁ is -N-C-S-R₁₀, R₁₀ is optionally substituted by hydrogen.



when R₁ is -C-R₁₀ the C atom is optionally substituted by oxo,

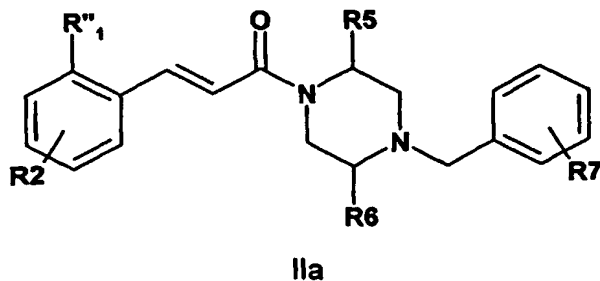
when R₁ is -C-R₁₀, R₁₀ is 3-oxa-1-aza-spiro[4.4]nonan-2-one, hydroxy, optionally substituted pyrrolidinyl, morpholino, piperazinyl, formic acid methyl ester, [1,2,4]triazol, imidazolidinyl, tetrazolyl, -N(CH₃)-OCH₃ or methoxy.

when R₁ is -C-R₁₀, R₁₀ is optionally substituted by hydrogen, oxo, methyl, acetyl, isopropyl, methoxy, hydroxy, formic acid methyl ester, dimethylamino or ethanone.

The optional substituents on R₁₀ are one or more substituents independently selected from the group consisting of hydrogen, or optionally substituted oxy, lower alkyl, carbonyl, amino; Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen, or optionally substituted oxy;

Wherein the optionally substituted substituents are optionally substituted once or more by a substituent independently selected from the group consisting of hydrogen or optionally substituted lower alkyl;

3. A compound of formula IIa, or a pharmaceutically acceptable salt or ester thereof,

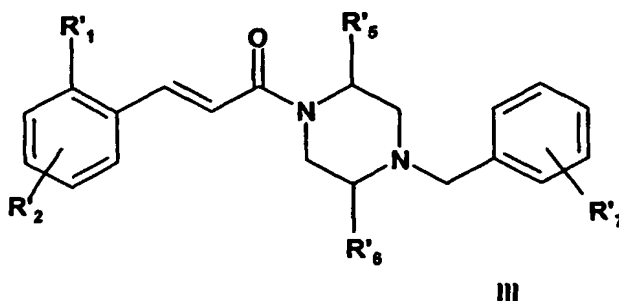


Wherein

R''_1 is $-NR''_{11}R''_{12}$

Wherein $-NR''_{11}R''_{12}$ collectively represents imidazolidinyl-2,4-dione, optionally substituted once or twice by a lower alkyl group.

4. A compound of formula III, or a pharmaceutically acceptable salt or ester thereof,



Wherein R'_1 is as herein before defined.

R'_2 and R'_7 are hydrogen, cyano, halo, butadienyl, methoxy, ethoxy, 2-methoxyethoxy, morpholino, trifluoromethoxy, 2-methylpropoxy, 2-propoxy.

R'_5 and R'_6 are independently selected from the group consisting of hydrogen and lower alkyl, acetyl;

5. A compound according to claim 1 selected from the examples 1-113 as disclosed in the specification.
6. A method of inhibiting chemokine receptors or of reducing inflammation in a subject (i.e., a mammal, especially a human) in need of such treatment which method comprises administering to said subject an effective amount of a compound according to claim 1, or a method of treating any of the above mentioned conditions, particularly a method of treating an inflammatory or autoimmune disease or condition, e.g., multiple sclerosis or rheumatoid arthritis, or alleviating one or more symptoms of any of the above mentioned conditions;

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a compound according to claim 1 for use as a pharmaceutical, e.g. for use as an immunosuppressant or antiinflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune or inflammatory disease or condition;

A pharmaceutical composition comprising a compound according to claim 1 in association with a pharmaceutically acceptable diluent or carrier, e.g., for use as an immunosuppressant or anti-inflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune or inflammatory disease or condition, or

use of a compound according to claim 1 in the manufacture of a medicament for use as an immunosuppressant or anti-inflammatory agent or for use in the prevention, amelioration or treatment of any disease or condition as described above, e.g., an autoimmune of inflammatory disease or condition.

7. A process for the preparation of a compound of formula I.

8. All novel compounds, methods, processes and uses substantially as hereinbefore described with particular reference to the Examples.